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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/520,769      | 07/13/2005  | Gerhard Hoeffle      | 930008-2194         | 5104             |

7590 04/02/2007  
Ronald R Santucci  
Frommer Lawrence & Haug  
745 Fifth Avenue  
New York, NY 10151

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| EXAMINER |
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KOSACK, JOSEPH R

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| ART UNIT | PAPER NUMBER |
|----------|--------------|

1626

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE  | DELIVERY MODE |
|--|------------|---------------|
| 3 MONTHS                               | 04/02/2007 | PAPER         |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

|                              |                                      |                                      |  |
|------------------------------|--------------------------------------|--------------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/520,769 | <b>Applicant(s)</b><br>HOEFLE ET AL. |  |
|                              | <b>Examiner</b><br>Joseph Kosack     | <b>Art Unit</b><br>1626              |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 01 February 2007.
- 2a) ☐ This action is FINAL.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1 and 3-14 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 3-12 and 14 is/are rejected.
- 7) ☒ Claim(s) 13 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Claims 1, 3-11, and 13-14 are pending in the instant application.

#### ***Amendments***

The amendment filed February 1, 2007 has been acknowledged and has been entered into the application file.

#### ***Election/Restrictions***

Applicant has acknowledged the election with traverse of Group I (claims 1-12) made telephonically on August 2, 2006. Applicant has traversed the requirement on the grounds that the groups are related as intermediate and final product. Applicant's traversal is granted in part in that Group IV (claims 13 and 14 in part) will now be examined with Group I. Groups II and III will not be examined as they not have the same basic chemical structure as the final product and the intermediates do not incorporate an essential structural element into the final product as they do not contain the framework for the *entire* thia-epothilone ring structure. Therefore, Group IV will now merge with Group I such that Group I is claims 1-12 (in full) and 13-14 (in part); Group II is claims 13-14 (in part); and Group III is claims 13-14 (in part). The restriction requirement as modified above is made FINAL.

#### ***Previous Claim Rejections - 35 USC § 112***

Claims 1-12 were rejected in the previous action under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Applicant's amendments and arguments were found to be persuasive and the rejection is withdrawn.

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Claims 11-12 were rejected in the previous action under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating some cancers, does not reasonably provide enablement for treating all cancers. Applicant's amendments and arguments were found to be persuasive and the rejection is withdrawn.

Claims 1-12 were rejected in the previous action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant's amendments and arguments were found to be persuasive and the rejection is withdrawn.

***Previous Claim Rejections - 35 USC § 103***

Claims 1-12 were rejected in the previous action under 35 U.S.C. 103(a) as being obvious over Nicolaou et al. (*Angew. Chem. Int. Ed.* 1998, 2014-2045) in view of Patani et al. (*Chem. Rev.* 1996, 3147-3176).

Applicant has traversed the rejection on the grounds that the C-5 carbonyl is essential to the function of the molecule and that even if it was not, the motivation to make the change would not be there due to the difficulty of synthesis. While Applicant's position is well taken, this is not found to be persuasive because Patani et al. teaches additionally that sulfoxide and sulfone moieties have increasingly been used as nonclassical divalent bioisosteres of the carbonyl group. See page 3167, column 2. Additionally, Patani et al. state that sulfoxides and sulfones are recognized as nonclassical bioisosteres suitable for replacement of a carbonyl group, thioethers are not. See page 3167, column 1. The Examiner had originally misread Patani et al. to

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read that sulfoxides and sulfones were not looked upon as a suitable replacement for a carbonyl except when the position is non-essential to the binding of the molecule to a receptor. Patani et al. clearly teaches that the replacement is art-recognized and the use of the replacement is growing. The rejection is maintained with the exception of claim 2 which is withdrawn as that claim is cancelled..

### ***Previous Double Patenting Rejections***

Claims 12-23 were provisionally rejected in the previous action on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12 and 22 of copending Application No. 10/535,474, now published as UPSN 20060128966 A1 in view of Patani et al. (*Chem. Rev.* 1996, 3147-3176). This is a typographical error by the Examiner and was meant to read claims 1-12 provisionally rejected and not 12-23.

It is noted that Applicant is considering a terminal disclaimer once the claims become otherwise allowable. As there is a maintained rejection and no terminal disclaimer yet on file. The provisional rejection is maintained with the exception of claim 2 which is withdrawn as that claim is cancelled. Applicant is reminded that since the instant case is the senior case, a terminal disclaimer may not be needed once all other rejections are withdrawn.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

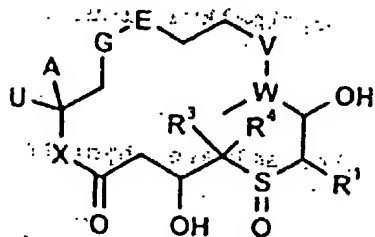
The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 3-12 rejected under 35 U.S.C. 103(a) as being obvious over Nicolaou et al. (*Angew. Chem. Int. Ed.* 1998, 2014-2045) in view of Patani et al. (*Chem. Rev.* 1996, 3147-3176).

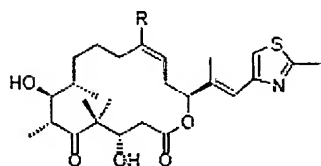
The instant application is drawn to compounds of the formula:



with substitutions as defined along with a method of treating cancer with the compounds.

Determination of the scope and content of the prior art (MPEP §2141.01)

Nicolaou et al. teach Epothilone D which as the structure of



where R is methyl. Nicolaou et al. also teach the use of epothilones to treat cancer by killing tumor cells through a mechanism similar to paclitaxel. See page 2016.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Nicolaou et al. do not teach a SO in place of the carbonyl next to the gem-dimethyl of the epothilone ring.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

Patani et al. teach that carbonyl can be replaced by SO and that the change has been used increasingly in the pharmaceutical art. See page 3167, Figure 67, Table 39, and the last paragraph of column 1 to the end of the first full paragraph of column 2.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention was made to follow the synthetic scheme of Nicolaou et al.

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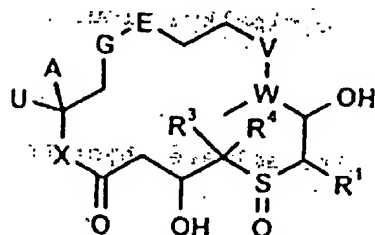
with the replacement suggested by Patani et al. to make the claimed invention. The motivation to do so is provided by Nicolaou et al. Nicolaou et al. teach the use of the compounds as killers of tumor cells. See page 2016.

Thus, the claimed invention as a whole was *prima facie* obviousness over the combined teachings of the prior art.

### ***Double Patenting***

Claims 1 and 3-12 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12 and 22 of copending Application No. 10/535,474, now published as UPSN 20060128966 A1 in view of Patani et al. (*Chem. Rev.* 1996, 3147-3176).

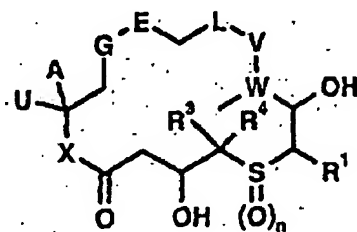
The instant application is drawn to compounds of the formula:



with substitutions as defined along with a method of

treating cancer with the compounds.

### **Determination of the scope and content of the prior art (MPEP §2141.01)**



'474 teaches compounds of the formula

with

substitutions as defined.



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Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

'474 does not teach a SO in place of the S or SO<sub>2</sub> group in the compound.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

Patani et al. teach that carbonyl can be replaced by S, SO, or SO<sub>2</sub> if the position is not essential to the function of the molecule. See page 3167, Figure 67, Table 39, and the last paragraph of column 1.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention was made to follow the synthetic scheme of '474 with the replacement suggested by Patani et al. to make the claimed invention. The motivation to do so is provided by '474. '474 teaches the use of the compounds to treat cancer. See claim 11.

Thus, the claimed invention as a whole was *prima facie* obviousness over the combined teachings of the prior art.

This is a provisional obviousness-type double patenting rejection.

*The following new objection and rejections are not necessitated by amendment.*

***Claim Objections***

Claims 13 and 14 are objected to for containing elected and non-elected subject matter. The elected subject matter have been identified supra.

***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

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Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 14 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 14 provides for the use of compounds of claim 13, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

### ***Conclusion***

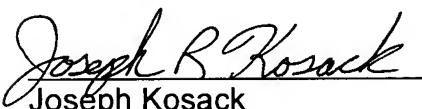
Claims 1, 2-12, and 14 are rejected. Claims 13 and 14 are objected to. Claims 13 and 14 are free of the art.

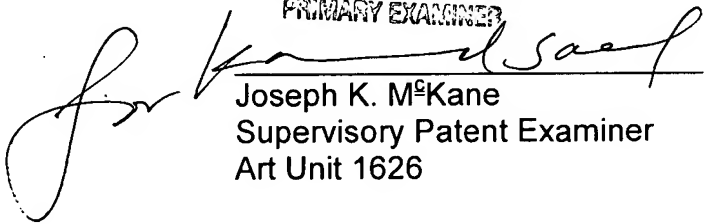
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Kosack whose telephone number is (571)-272-5575. The examiner can normally be reached on M-F 5:30 A.M. until 2:00 P.M.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph M<sup>o</sup>Kane can be reached on (571)-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Joseph Kosack  
Patent Examiner  
Art Unit 1626

  
KAMLA A. SAIED, Ph.D.  
PRIMARY EXAMINER  
Joseph K. M<sup>o</sup>Kane  
Supervisory Patent Examiner  
Art Unit 1626